

## Hot Topics Scholarship Advocate Reports from the 2007 San Antonio Breast Cancer Symposium

Topic: Bone health

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## Biophosphonates are showing promise for bone loss associated with estrogen blockers in breast cancer treatment.

Bone loss is a major side effect of estrogen blockers and aromatase inhibitors. Treatments such as Arimidex, Femara, Chemotherapy and others that are utilized by women with breast cancer can have a serious toll on the bone health of patients. Researchers wanted to know if the bone loss associated with many of these standard treatments can be reversed or prevented by using bisphosphonate drugs during these therapies.

Researchers presenting two different papers at the 2007 San Antonio Breast Cancer Symposium showed that bone loss due to these treatments can be reduced using Zometa or zoledronic acid and preliminary studies are showing that by giving these drugs in combination with other treatments bone loss can be prevented.

Results of the trials (ABCSCG-12 and ZFast) were similar, partial recovery of bone loss by about 6% after 3 years. Recovery seems to be due to receiving bisphosphonates 2 times per year via IV infusion, since these drugs are poorly tolerated orally. After five years the Arimidex/Femara group of patients saw an increase or prevention of bone loss of between 7.8%-13.6% and the tamoxifen group saw a 5% decrease or suppression in bone loss. Patients who received zoledronic acid (ZA) showed unchanged bone mineral density at 36 months compared to those untreated who showed impaired bone mineral density. The trials were randomized with Zometa vs. No Zometa. Most of the subjects were older than 40 years, Stage I, II & III, and all had 3 years of endocrine treatment for Estrogen and Progesterone positive tumors. Both studies showed there was no statistically significant change in fracture rates.

This is encouraging news for many breast cancer patients who are concerned with bone loss; however, bisphosphonates have their own set of side effects, including a first infusion effect, which can cause fever and general malaise, and there were some toxicity and renal problems as well as a risk of osteonecrosis of the jaw. Also, affordability may be an issue since it is a fairly costly treatment.

It is hopeful to know that science is reaching towards an effective therapy for people who become osteopenic during treatment with endocrine therapy.

Many experts agree that as long as patients follow guidelines for osteoporosis, including seeing their doctor and assessing BMD (bone mineral density) every two years, there is no need for excessive worry about the bone loss associated with aromatase inhibitors and other treatments for breast cancer.

These findings<sup>1</sup> presented at 2007's Annual Symposium leave many asking, "Should bisphosphonates be considered in standard treatment for breast cancer patients who are both estrogen and progesterone positive and receiving hormone therapy?"

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<sup>1</sup> SABCS: 2007 Abstract #26, ABCSG; Austrian Breast and Colorectal Cancer Study Group, Vienna, Austria.  
SABCS: 2007 Abstract #27 Z-FAST Study Group; Novartis Pharmaceuticals, East Hanover, NJ

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## BONE HEALTH DURING and AFTER TREATMENT

### **Making decisions about breast cancer treatments**

Treatment for breast cancer always requires making decisions between the choices of available and appropriate medications and modalities. Traditionally the physician and health care personnel made the decisions and the patient was a passive recipient. Breast cancer patients have, for many years now, been an educated group who participate in the decisions regarding treatment. Advocates play an important role both in influencing the regulatory, pharmaceutical and health services communities, and in educating and supporting the patients. After attending the poster and presentation sessions at the San Antonio Breast Cancer Symposium this year, and reading the literature regarding bone health during and after breast cancer treatment, it reinforced for me that one must always consider the quality of life of the patient when considering the treatment implications. Some new findings regarding bone health and damage with breast cancer treatment pharmaceuticals give one pause to consider the treatment alternatives and the issues related to osteoporosis and osteopenia and how they affect lifespan and the quality of life.

### **Some breast cancer treatments affect bone health but there are some treatments**

Estrogens are produced in the ovaries and other body tissues using substances called aromatases. In post-menopausal women the ovaries are no longer producing estrogen; however the adrenals and other sites, with the support of the aromatases, can and do still produce estrogen. In post-menopausal women who, after treatment with tamoxifen have a recurrence of breast cancer, treatment with an aromatase inhibitor (AI) leads to a decrease in circulating estrogen which leads to a decrease in tumor size or delayed progression of tumor growth. The AI Arimidex, in studies, significantly reduced the risk of breast cancer returning compared with tamoxifen. While the AI's appear to be effective in keeping tumor growth at bay, there are studies which indicate that the reduction of estrogen causes bone thinning, which could lead to an increase in the incidence of osteopenia and osteoporosis.

In abstract #28: Effect of anastrozole on bone mineral density (BMD) after one year of treatment: results from bone sub-study of the International Breast Cancer Intervention Study (IBIS-II), reported that women who were treated with bisphosphonate risedronate for one year had an increase in bone mineral density, which would lead to a reduction in spontaneous fractures. Bisphosphonates are a class of drugs that inhibit osteoclasts, a type of bone cell, that removes bone tissue from the soft tissues within the bone structure. This is a process known as bone resorption, which results in a transfer of calcium from bone fluid to the blood.

In abstract #47: In a phase 3 study of the effect of denosumab therapy on bone mineral density in women receiving aromatase inhibitors for non-metastatic breast cancer, we learned of the dramatic changes in bone physiology with an increase in bone mineral density which reduces fractures and improves the quality of life of these patients. Denosumab, a human monoclonal antibody which is used to treat osteoporosis, is given twice yearly in subcutaneous (the layer just under the outer skin) injections. Denosumab's mode of administration makes it an important alternative to those who cannot tolerate bisphosphonates. Denosumab is being studied for its potential in a broad range of bone loss conditions including osteoporosis, treatment-induced bone loss, bone metastases, multiple myeloma and rheumatoid arthritis.

Additional reading has shown that bisphosphonates have at least 4 potential uses in women with breast cancer:

- \*Preventing or delaying skeletal complications in patients with documented bone metastases
- \*Palliation (reduction) of bone pain
- \*Delaying the appearance of bone metastases in patients with high-risk early stage disease
- \*prevention of the bone loss that accompanies adjuvant systemic therapy

A fifth reason for giving women bisphosphonates is that some scientists believe that this class of drugs could make bones less friendly to cancer cells. This idea needs further study.

Experts are working on guidelines for prescribing bisphosphonates as a preventive agent with aromatase inhibitors, with paying particular attention to a woman's risk for osteoporosis and fractures.

### **Osteoporosis: Breast cancer treatments and this public health problem**

Osteoporosis is a [disease](#) of [bone](#) leading to an increase in fractures. In osteoporosis the [bone mineral density](#) (BMD) is reduced. Osteoporotic fractures are an important public health problem that contributes to morbidity and mortality, especially in a world with an ageing population, and, in this context, to women who are pre and post menopausal and are being treated for breast cancer with aromatase inhibitors. The aim of treatment is to prevent the development of osteoporosis and to prevent further bone loss in order to decrease the risk of osteoporotic fractures. We currently have several different types of drugs to treat osteoporosis.

They are:

- \*antiresorptive drugs slow the progressive thinning of bone (bisphosphonates, estrogen derivatives, calcitonin, etc.)
- \* bone forming drugs help to rebuild the skeleton
- \*other drugs with more complex action such as denosumab and otehrs.

In addition, calcium and vitamin D supplements might also be prescribed.

Other lifestyle and non-pharmacologic approaches include diet, exercise, and cessation of smoking.

## **Conclusion**

Osteoporosis can cause a painful existence and it may shorten lifespan, so it is important to consider quality of life when making decisions about breast cancer treatment.

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Abstract #28: Effect of anastrozole on bone mineral density (BMD) after one year of treatment: results from bone sub-study of the International Breast Cancer Intervention Study (IBIS-II). Shalini Singh, Jack Cuzick, Rob Edwards, Glen Blake, John Truscott, R Coleman, Richard Eastell, and Anthony Howell

Abstract #47: A phase 3 study of the effect of denosumab therapy on bone mineral density in women receiving aromatase inhibitors for non-metastatic breast cancer. Ellis, G., Bone, HG, Chlebowski, R, Paul, D., Spadafora, S., Smith, J., Fan, M., and Jun,S.